model. Analyses limiting the dementia outcome to AD alone (45 cases) had essentially the same results. **Conclusions:** These findings suggest that WMH may interfere with cognitive function but may not be sufficient to produce dementia. In persons whose cognitive abilities are already impaired, a global measure of brain atrophy is more predictive of conversion to dementia. Persons at increased risk of stroke are also at increased risk of dementia.

P2-358 COGNITIVE PROCESSING SPEED AND MYELIN BREAKDOWN IN OLDER INDIVIDUALS

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Background: The process of myelination peaks in middle age followed by myelin breakdown and loss. Investigations of information processing speed performance across the lifespan reveal a trajectory that parallels myelination and subsequent myelin breakdown. Myelin breakdown may result in a progressive "disconnection" of widely distributed neural networks and may underlie age-related cognitive decline and Alzheimer's disease (AD). **Objective(s):** This study tests the "myelin model"/hypothesis that in older individuals, myelin breakdown in late-myelinating regions is associated with slowed processing speed and contributes to the continuum of cognitive decline that ultimately results in AD. **Methods:** Healthy older (>55 years) individuals (N=92) and 8 subjects with Alzheimer's disease (AD) had neurocognitive testing. The late-myelinating frontal lobe white matter (Fwm) as well as early- and later-myelinating regions of the corpus callosum, the splenium (Swm) and genu (Gwm) respectively, were assessed using MRI and transverse relaxation rates (R_2) were calculated. R_2 is an indirect measure of white matter structural integrity; it declines with age-related myelin breakdown and is significantly lower in AD. **Results:** As hypothesized, cognitive processing speed tasks (Trails A and Digit Symbol) were significantly associated with R_2 in late-myelinating regions (Fwm, $p<.0001$ and Gwm, $p<.004$) but not in the early myelinating Swm region ($p>.2$). **Conclusions:** These data suggest that myelin breakdown in healthy older individuals underlies the age-related cognitive decline that ultimately results in AD. MRI measures of myelin breakdown and cognitive measures may be useful in AD primary prevention studies.

P2-359 PREDICTING COGNITIVE DECLINE IN MCI AND HEALTHY AGING WITH STRUCTURAL AND PERFUSION MRI AND MRS

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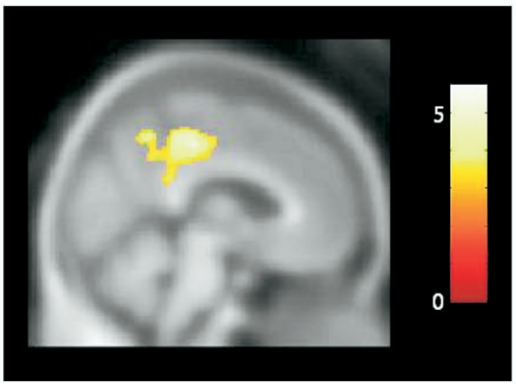
Background: Potentially effective treatments for Alzheimer's disease (AD) are beginning to enter human trials. Thus, it is important to develop measurements that can predict cognitive decline in mildly impaired subjects so that individuals at greatest risk for AD can be targeted when preventative treatments do become available. **Objective:** To determine the regional pattern of structural, perfusion, and metabolic changes in the brain that predict cognitive decline. **Methods:** Fifty-five subjects (75.1 ± 7 years old) were assessed with neuropsychological tests at baseline and 1.2 ± 0.2 years later. Forty-eight subjects were MCI patients and 7 were healthy controls. Multiple regression was used to investigate the relationship between baseline cognition, volumetric structural MRI data (available for 45 subjects), and ^{1}H MRS data (42 subjects) and cognitive decline. Separate regressions were computed for change in MMSE, CDR, CDR sum of boxes, and different California Verbal Learning Test (CVLT) measures. Baseline measures were dependent variables, cognitive change scores were independent variables, and age, group, and test interval were nuisance variables in the analyses. The relationship between baseline cerebral perfusion, as determined by arterial spin labeled MRI (33 subjects) and cognitive decline were assessed with SPM2. **Results:** Baseline CVLT measures were negatively associated with in MMSE, CDR, and CDR sum of boxes change scores (i.e., lower baseline scores associated with greater decline, $p<0.05$). Baseline frontal and parietal gray matter (GM) volumes were also negatively associated with MMSE decline ($p<0.01$). Adding baseline frontal and parietal GM volumes to baseline CVLT measures significantly improved (p 0.03) the linear model. Baseline posterior cingulate N-acetylaspartate (NAA)/creatine (Cr) ratio was negatively associated with decline in CDR sum of boxes ($p<0.05$). However, adding NAA/Cr ratio to baseline CVLT measures did not improve the linear model for predicting CDR sum of boxes decline. Voxel-by-voxel analyses revealed a negative relationship between baseline cerebral perfusion in the posterior cingulate and subsequent decline on CVLT short delay cued recall, even after accounting for baseline CVLT performance (see Figure 1). **Conclusions:** These preliminary results suggest that arterial spin labeled MRI and volumetric structural MRI may add predictive value to neuropsychological testing for predicting cognitive decline.

Figure 1. Regions showing significant correlations between perfusion and subsequent decline on CVLT short-delay cued recall, $p<0.05$, corrected for multiple comparions.



P2-360 CORTICAL THINNING IN ALZHEIMER'S DISEASE AND FRONTOTEMPORAL DEMENTIA

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Background: Volumetric MRI studies show characteristic patterns of brain atrophy in Alzheimer's disease (AD) and frontotemporal dementia (FTD); however, an overlap between the groups remains. In contrast to general brain tissue loss, pathological studies reported predominantly loss of cortical layers in dementia, resulting in cortical thinning. Recently, MRI studies have used cortical thickness to better characterize brain alterations in dementia. **Objectives:** 1) To compare the regional patterns of cortical thinning in AD and FTD; 2) To determine if cortical thickness is a better measure than cortical volume to differentiate between normal aging, AD and FTD. **Methods:** 23 cognitive normal (CN) subjects, 21 AD and 19 FTD patients had MRI at 1.5T. Measurements of cortical thickness and volume were performed using FreeSurfer (http://surfer.nmr.mgh.harvard.edu). Regional differences in cortical thickness between the groups were tested vertex-by-vertex. The powers of cortical thickness and volume measures in frontal, parietal and temporal lobes to classify the groups were compared using logistic regression and receiver operator characteristics (ROC) analyses. **Results:** The figure depicts statistical maps of differences in cortical thinning between the groups. Compared to CN, AD was associated with thinner cortices in temporal, parietal and frontal regions, precuneus and posterior cingulate ($p<0.001$), while FTD was associated with thinner cortices in primarily frontal and temporal regions ($p<0.001$). Com-